REMARKS

I. Status of the Claims

Claims 1-58 are pending in the application. Claims 9, 10, 21-27, 31-40 and 43-58 have been withdrawn from consideration by the Examiner as being drawn to a non-elected invention. Claim 1 has been amended to more particularly recite that neuromuscular dysfunction of the lower urinary tract is what is being effectively treated. The scope of claim 1 is unchanged by this amendment. To the extent support for this amendment is needed, it can be found throughout the specification, *e.g.,* at page 50, lines 6-19. Claims 3-6 have been amended to correct the spelling of "selectivity."

By this Amendment, no new matter has been added to the application.

II. Objections to the Claims

The Examiner has objected to claims 3-6 because the word "selectivity" is misspelled. The spelling of "selectivity" has been corrected. Withdrawal of the objection is requested.

II. Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 1-8, 11-20, 28-30 and 41-42 for alleged indefiniteness. The Examiner contends that the claims are indefinite because it is not clear what conditions, diseases or disorders of the host are being treated.

In response, claim 1 has been amended to recite that the amount of a compound having selective affinity for the mGlu5 subtype of glutamate receptors is effective to treat neuromuscular dysfunction of the lower urinary tract. Support for this amendment can be found throughout the specification, and particularly at page 50, lines 6-19. The amendment does not change the scope of claim 1.

The amendment to claim 1 is believed to address the present rejection by further clarifying what conditions, diseases or disorders of the host are being treated. Reconsideration of

the claims 1-8, 11-20, 28-30 and 41-42 and withdrawal of the rejection thereof under 35 U.S.C. § 112, second paragraph is requested.

III. Claim Rejections under 35 U.S.C. § 103(a)

The Examiner has rejected claims 1-8, 11-20, 28-30, 41 and 42 as allegedly being obvious over WO 2001/16121 to Cosford *et al.* ("Cosford") in view of Bonney *et al.* (1997) "Bladder Dysfunction in Schizophrenia," *Schizophrenia Research* 25:243-49 ("Bonney") and Nilvebrandt (2001) "Clinical Experiences with Tolterodine," *Life Sciences* 68:2549-56 ("Nilvebrandt").

According to the Examiner, Cosford teaches compounds of the formula A-L-B, including MTEP (3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine), compositions thereof to be administered by a variety of routes, and that the compounds are useful for treating diseases such as schizophrenia. The Examiner further asserts the dosage amounts called for in the claims are obvious over Cosford.

The Examiner acknowledges that Cosford does not teach or suggest using the disclosed compounds to treat any condition associated with neuromuscular dysfunction of the lower urinary tract. Thus, the Examiner cites Bonney to attempt to remedy the deficiencies of Cosford. According to the Examiner, Bonney teaches that there is a correlation between schizophrenia and bladder dysfunction/incontinence and that similar brain abnormalities are associated with both conditions. The Examiner's position is that, based on the alleged correlation of schizophrenia and bladder incontinence taught in Bonney, one skilled in the art would have reasonably expected that Cosford's compounds, which can be used to treat schizophrenia, would also successfully treat urinary incontinence. Finally, the Examiner cites Nilvebrandt for disclosing that tolterodine is a non-selective muscarinic receptor antagonist for the treatment of overactive bladder, and that its efficacy is equal to that of oxybutynin. The Examiner argues that one of ordinary skill in the art would have been motivated to combine the pharmaceutical compositions of Cosford with the

muscarinic receptor antagonist of Nilvebrandt with a reasonable expectation of success because each was known to be useful for the same therapeutic purpose – treatment of urinary incontinence.

The rejection is traversed on the ground that there is not motivation to combine Cosford and Bonney. Obviousness based on a plurality of references requires a motivation to combine the references and a reasonable expectation of success. In the present case, there is no motivation to combine Cosford with Bonney or a reasonable expectation that drugs used to treat schizophrenia could reasonably be expected to treat lower urinary tract dysfunction. Bonney merely describes that urinary incontinence is a symptom associated with schizophrenia in some instances. Bonney makes no suggestion that agents used to treats schizophrenia would or could be used to treat incontinence. To the contrary, a closer reading of Bonney shows that the authors considered treatment of schizophrenia and incontinence to be two separate problems, subject to treatment by different classes of agents. Thus, Bonney discloses that psychiatric medication used to treat schizophrenia may contribute to incontinence. ("It is notable that incontinence accompanies neuroleptic drug treatment (Ambrosini, 1984), which selectively blocks dopamine receptors in the basal ganglia (Gur and Pearlson, 1993)." Bonney at page 248, col. 1, second full paragraph). Bonney further discloses that the high prevalence of detrusor hyperreflexia (DH) in schizophrenic patients means that "awareness of this situation will lead to . . . appropriate treatment of incontinence." Bonney at page 248, col. 2, second full paragraph. The fact that Bonney lists schizophrenia medication as a possible cause of incontinence and indicates that schizophrenic patients can receive "appropriate" treatment only after being identified as having detrusor hyperreflexia shows that Bonney does not consider agents useful for treating schizophrenia to also be useful for treating lower urinary tract disease. Thus, when viewed fairly and as a whole, Bonney's disclosure that lower urinary tract disease may in some instances be associated with schizophrenia does not lead to the suggestion that drugs used to treat schizophrenia could or should be used to treat lower urinary tract dysfunction. Thus, the Examiner's rationale for combining Cosford and Bonney fails. For at least this reason, the obviousness rejections should be withdrawn.

Nilvebrandt teaches only the use of tolterodine to treat overactive bladder. Accordingly, Nilvebrandt does not remedy the deficiencies of either Cosford or Bonney.

For the reasons set forth above, Applicants submit that claims 1-8, 11-20, 28-30, 41 and 42 are not obvious over Cosford in view of Bonney and Nilvebrandt. Reconsideration of these claims and withdrawal of the rejection thereof under 35 U.S.C. § 103(a) is requested.

IV. Conclusion

This application is believed to be in condition for allowance, which is earnestly solicited.

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Respectfully submitted,

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